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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Takayoshi Mamine

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EXAMINER

BABIC, CHRISTOPHER M

ART UNIT

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1637

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/529,949	Applicant(s) MAMINE ET AL.	
	Examiner CHRISTOPHER M. BABIC	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) 5-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Claim(s) 1-18 are pending. Claim(s) 1-4 are under examination. The following Office Action is in response to Applicant's communication dated February 17, 2009.

Claim Rejections - 35 USC § 103 - Maintained

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claim(s) 1, 3, and 4 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Quate et al. (U.S. 6,203,983 B1) in view of Washizu et al.

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("Electrostatic manipulation of DNA in microfabricated structures," IEEE Trans. Ind. Applicat., vol. 26, pp. 1165-1172, 1990), and in further view of Wachter et al. (U.S. 5,445,008), and in further view of Daratchiev et al. (U.S. 6,457,360 B1).

With regard to claims 1 and 3, Quate teaches methods for detecting hybridization of target nucleic acids (fig. 1-4; col. 5-6, for example) comprising: providing a cantilever comprising immobilized oligonucleotides (fig. 1, 11; col. 4, lines 25-40, for example); introducing a sample comprising oligonucleotides complementary to that of those immobilized on the cantilever (col. 4, lines 25-40, for example); and detecting hybridization based on a change in resonant frequency (col. 4, lines 25-40, for example).

Quate does not expressly teach forming an uneven electric field at the surface of immobilized oligonucleotides, actively vibrating and exciting the cantilever by using a driving source, or detecting the vibration amplitude of the cantilever by measuring a voltage of a resistor coupled with the cantilever.

With regard to the formation of an uneven electric field at the surface of immobilized oligonucleotides as well as claim 4, Washizu provides a supportive disclosure that teaches the application of an uneven electric field to immobilize and stretch DNA molecules (pg. 1166, section III, experimental method, for example). The reference expressly teaches that the methods can be used to neatly align DNA molecules on substrates within biosensors as well as position DNA molecules on the edge of strips or pinpoints (pg. 1171, col. 1, for example).

With regard to the vibration of the cantilever through the use of a driving force, Wachter provides a supportive disclosure that teaches actively vibrating and exciting a coated cantilever with a driving force (fig. 1, 10, 12, 14; col. 1, lines 45-end, for example), exposing a target compound to the oscillating cantilever (col. 1, lines 45-end, for example), and detecting the binding of the target to the cantilever by measuring change in resonant frequency (col. 1, lines 45-end; fig. 5, for example).

With regard to the vibration amplitude of the cantilever by measuring a voltage of a resistor coupled with the cantilever, Daraktchiev provides a supportive disclosure that teaches determining the resonance frequency of the free end of the cantilever by measuring an output voltage of the piezo-resistive detector element as a function of the frequency of the applied alternating current (col. 2, lines 15-45, for example). The reference further exemplifies such methods as providing high precision as compared to the prior art (col. 1, lines 30-45, for example).

Thus, in summary, it is submitted that it would have been *prima facie* obvious to a skilled artisan at the time of invention to utilize a driving source to vibrate the cantilever within Quake since the prior art demonstrates such a technique as useful for the detection of a target binding to a cantilever.

Furthermore, it would have been *prima facie* obvious to a skilled artisan at the time of invention to concentrate an uneven electric field at the immobilized oligonucleotides on the surface of the cantilever within the detection methods of Quake since the prior art suggests such a step to neatly align DNA molecules on the substrate.

Furthermore, it would have been *prima facie* obvious to a skilled artisan at the time of invention to incorporate a piezo-resistive element onto the cantilever within the detection methods of Quake to allow for the determination of cantilever vibration frequency since the prior art suggests such a step for high precision detection.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

First, with respect to the arguments regarding the teachings of Washizu, Applicant is reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Furthermore, the examiner is not asserting that the electrode disclosed in Washizu could constitute a cantilever. As cited above, Washizu is relied upon to demonstrate the application of an uneven electric field to surface immobilized polynucleotides.

Next, with respect to the arguments regarding the teachings of Daraktchiev, the detection of a resonance frequency as taught in Daratchiev necessarily encompasses the detection of an amplitude since a cantilever oscillation frequency cannot occur without a degree of cantilever oscillation amplitude. In other words, in order for a cantilever oscillation frequency to register a resistance value, a cantilever oscillation amplitude must take place. Thus, one detecting frequency is necessarily detecting amplitude. The examiner would agree that Daraktchiev does not expressly teach

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correlating a resistance value with a measurable unit of amplitude (e.g. peak amplitude distance of the cantilever); however such a measurement is not required by the claim.

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Thus, the rejection is maintained.

2. Claim(s) 2 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Quate et al. (U.S. 6,203,983 B1) in view of Washizu et al. ("Electrostatic manipulation of DNA in microfabricated structures," IEEE Trans. Ind. Applicat., vol. 26, pp. 1165-1172, 1990), and in further view of Wachter et al. (U.S. 5,445,008), and in further view of Daratchiev et al. (U.S. 6,457,360 B1) as applied to claim 1 above, and in further view of Yamamoto et al. (U.S. 5,268,571).

The teachings of the previously applied reference(s) have been outlined in the above rejections. The previously applied reference(s) do not expressly teach a cantilever having a piezoelectric material disposed between counter electrodes and subsequent vibration with application of AC voltage between the counter electrodes.

Yamamoto provides a supportive disclosure that teaches a microcantilever having a piezoelectric material disposed between counter electrodes and subsequent vibration with application of AC voltage between the counter electrodes (fig. 1; col. 4,

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lines 30-end, col. 5-6, example 1, for example). The reference shows the cantilever to have excellent responsiveness (col. 6, lines 25-35, for example).

Thus, in summary, it would have been *prima facie* obvious to a skilled artisan at the time of invention to utilize counter electrodes to vibrate a piezoelectric cantilever, such as those in Wachter, since the prior art demonstrates such a arrangement as useful for providing a cantilever with excellent responsiveness.

Response to Arguments

Applicant's arguments have been addressed in the response(s) set forth above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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